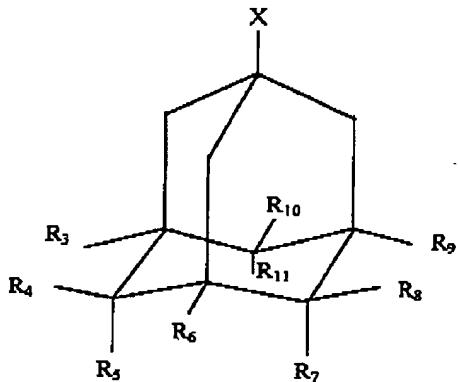


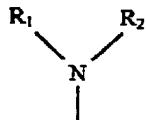
Appl. No. 10/016,850
Reply to Office Action of September 29, 2005

STATUS OF CLAIMS

1. (Previously presented) A topical ophthalmic composition comprising a carrier and a pharmaceutical conjugate comprising an ophthalmically useful therapeutic component covalently coupled to an efficacy enhancing component effective in delivering the conjugate to a posterior portion of an eye of an individual when the composition is topically administered to the eye, the efficacy enhancing component having the formula A:



wherein X is



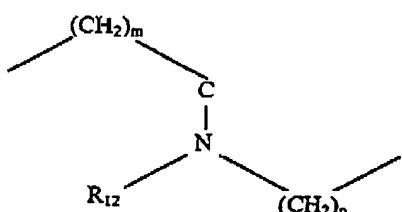
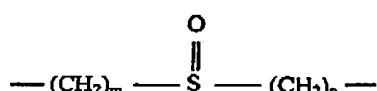
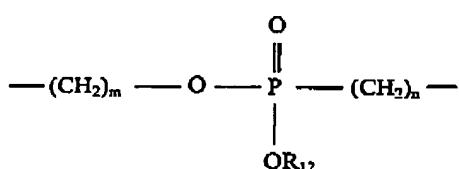
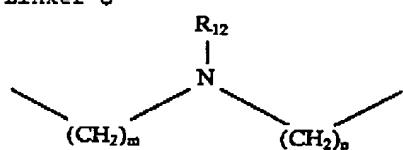
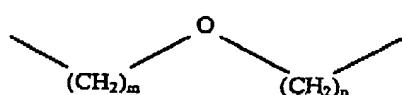
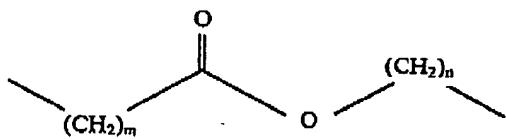
R1, R2, R3, R4, R5, R6, R7, R8, R9, R10 and R11 are independently an H, a C1-C10 hydrocarbon, or a linker.

2. (Previously presented) A composition of claim 1 wherein the therapeutic component and the efficacy enhancing component are directly joined by a covalent bond, and the carrier comprises a liquid.

**Appl. No. 10/016,850
Reply to Office Action of September 29, 2005**

3. (Previously presented) A composition of claim 1 wherein the therapeutic component and the efficacy enhancing component are joined by a linker.
4. (Previously presented) A composition of claim 1 wherein R1 and R2 are Hs, and R3 is a linker.
5. (Previously presented) A composition of claim 1 wherein the efficacy enhancing component is a memantine.
6. (Previously presented) A composition of claim 1 wherein the linker is selected from the group consisting of:

Appl. No. 10/016,850
Reply to Office Action of September 29, 2005



Appl. No. 10/016,850
Reply to Office Action of September 29, 2005

wherein R12 is an H or a Cl-C10 hydrocarbon, m = 0 to 10, and n = 0 to 10.

7. (Withdrawn) A pharmaceutical conjugate of claim 1 wherein the therapeutic component is selected from the group consisting of NMDA antagonists, antibacterials, antihistamines, decongestants, antiinflammatories, antiparasitics, miotics, anticholinergics, adrenergics, antivirals, local anesthetics, antifungals, amoebicidals, trichomonocidals, analgesics, mydriatics, antiglaucoma drugs, carbonic anhydrase inhibitors, ophthalmic diagnostic agents, ophthalmic agents used as adjuvants in surgery, chelating agents, antineoplastics, antihypertensives, muscle relaxants, diagnostics, tyrosine kinase inhibitors and neuroprotectants.

8. (Previously presented) A composition of claim 1 wherein the therapeutic component is selected from the group consisting of quinoxaline, (2-imidazolin-2-ylamino) quinoxaline, 5-bromo-6-(2-imidazolin-2-ylamino) quinoxaline, and mixtures thereof.

9. (Previously presented) A composition of claim 1 wherein the efficacy enhancing component comprises a memantine, and the conjugate further comprises a linker joining the therapeutic component and the memantine.

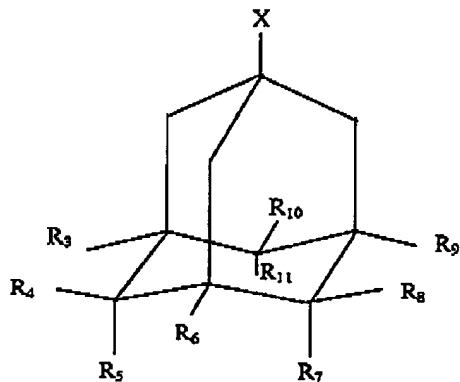
10. (Withdrawn) A pharmaceutical conjugate of claim 1 wherein the therapeutic component comprises a timolol and the efficacy enhancing component comprises a memantine, and the conjugate further comprises a linker joining the timolol and the memantine.

**Appl. No. 10/016,850
Reply to Office Action of September 29, 2005**

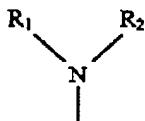
11. (Previously presented) A composition of claim 8 further comprising a memantine, and a linker joining the therapeutic component and the memantine.
12. (Previously presented) A composition of claim 1 wherein the therapeutic component and the efficacy enhancing component disassociate under physiological conditions.
13. (Cancelled)
14. (Previously presented) A composition of claim 1 wherein the conjugate has an aqueous solubility, a partition coefficient and/or an affinity for melanin that is greater relative to a compound comprising the same therapeutic component which is not joined to an efficacy enhancing component.
15. (Previously presented) A composition of claim 1 wherein the conjugate is a salt.

Appl. No. 10/016,850
Reply to Office Action of September 29, 2005

16. (Previously presented) A topical ophthalmic composition comprising a carrier and a pharmaceutical conjugate comprising an ophthalmically useful therapeutic component covalently coupled to an efficacy enhancing component effective in delivering the conjugate to a posterior portion of an eye of an individual when the composition is topically administered to the eye, the efficacy enhancing component having the formula A:

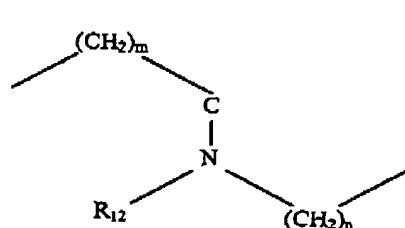
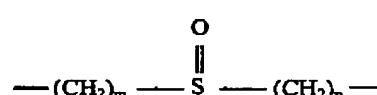
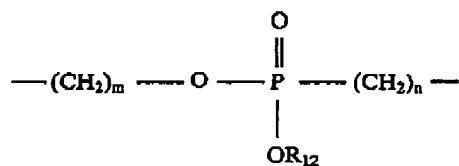
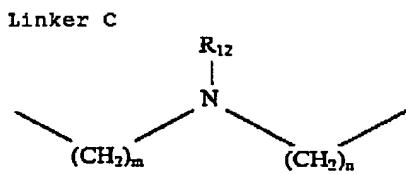
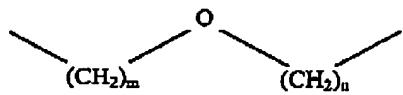
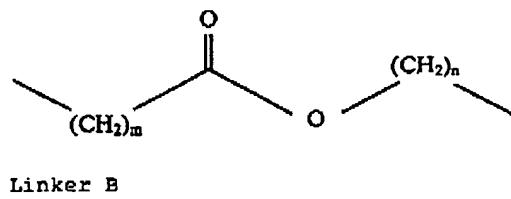


wherein X is



R₁, R₂, R₃, R₄, R₅, R₆, R₇, R₈, R₉, R₁₀ and R₁₁ are independently an H, a C₁-C₁₀ hydrocarbon, or a linker; the linker is selected from the group consisting of:

Appl. No. 10/016,850
Reply to Office Action of September 29, 2005

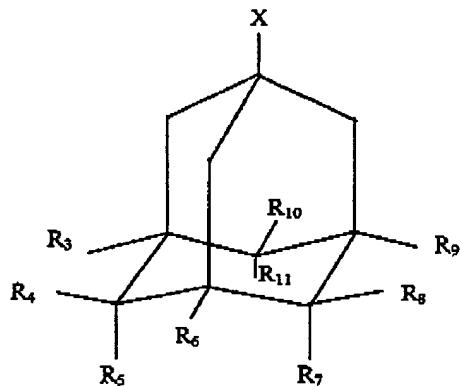


Appl. No. 10/016,850
Reply to Office Action of September 29, 2005

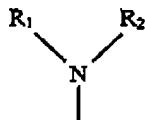
wherein R12 is an H or a C1-C10 hydrocarbon, m = 0 to 10, and n = 0 to 10.

17-23. (Cancelled)

24. (New) An ophthalmic composition comprising a carrier and a pharmaceutical conjugate comprising an ophthalmically useful quinoxoline component-containing therapeutic component covalently coupled to an efficacy enhancing component effective in delivering the conjugate to a posterior segment of an eye of an individual when the composition is topically administered to the eye, the efficacy enhancing component having the formula A:

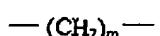
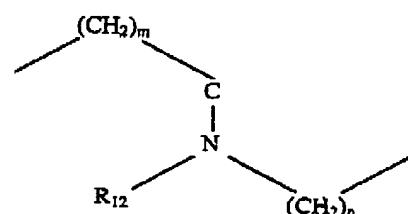
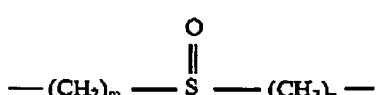
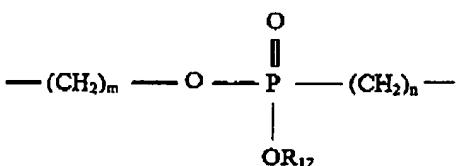
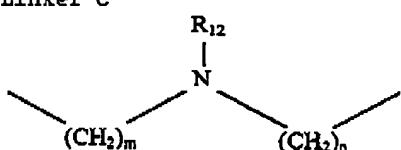
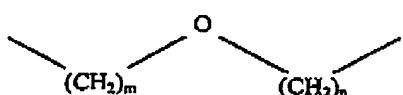
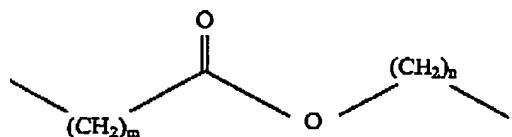


wherein X is



R1, R2, R3, R4, R5, R6, R7, R8, R9, R10 and R11 are independently an H, a C1-C10 hydrocarbon, or a linker; the linker is selected from the group consisting of:

Appl. No. 10/016,850
Reply to Office Action of September 29, 2005



Appl. No. 10/016,850
Reply to Office Action of September 29, 2005

wherein R12 is an H or a C1-C10 hydrocarbon, m = 0 to 10, and n = 0 to 10.

25. (New) The composition of claim 24 wherein the therapeutic component is selected from the group consisting of quinoxaline, (2-imidazolin-2-ylamino) quinoxaline, 5-bromo-6-(2-imidazolin-2-ylamino) quinoxaline, and mixtures thereof.

26. (New) The composition of claim 25 wherein the therapeutic component comprises brimonidine tartrate.